UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/759,519	01/16/2004	Charles R. Cantor	701586-53651	7045

50607 7590 07/28/2008

RONALD I. EISENSTEIN
100 SUMMER STREET
NIXON PEABODY LLP
BOSTON, MA 02110

EXAMINER	
KAPUSHOC, STEPHEN THOMAS	
ART UNIT	PAPER NUMBER
1634	
MAIL DATE	DELIVERY MODE
07/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/759,519	CANTOR ET AL.	
	Examiner	Art Unit	
	Stephen Kapushoc	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,9,12,15-17 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,9,12,15-17 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/09/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3-6, 9, 12, 15-17 and 20 are pending and examined on the merits.

Please note: the text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This Office Action is in reply to Applicants' correspondence of 5/9/2008.

Applicants' remarks and amendments have been fully and carefully considered but are not found to be sufficient to put this application in condition for allowance. Any new grounds of rejection presented in this Office Action are necessitated by Applicants' amendments. Any rejections or objections not reiterated herein have been withdrawn in light of the amendments to the claims or as discussed in this Office Action.

This Action is **FINAL**.

New Claim Rejections - 35 USC § 112 1st ¶ - New Matter

1. Claim 20 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 20 requires that primer pairs of the methods 'amplify a short amplicon of about 50 to about 100 base pairs'. The claim thus appears to limit the size of an amplicon produced to a lower size limit of 'about 50' base pairs, and to an upper size limit of 'about 100' base pairs. The Remarks indicate that basis for this limitation may be found in the specification at paragraph [015]. However, paragraph [015] states only the particular ranges (i.e. upper and lower limits) of 'about 90-350 bp' and 'about 100-250 bp'. These ranges a not indicative of the particular range set forth in the claim.

Further, paragraph [015] sets forth a series of lower limits for amplicon size, of 50, 100, 200, 300, 400m 500, 600-1000 bp and up to about 10000bp. However this recitation in the instant specificaiton does not set forth any desired upper limit to the size of the amplicon, where as the claim limitation of 'a short amplicon of about 50 to about 100 base pairs' sets forth the required upper limit of the amplicon. Further it is noted that this portion of the specification of 10/759,519 is not present in the priority document (e.g. paragraph [011] of provisional application 60/441,046).

The specific limitations of the rejected claim are not set forth either explicitly or implicitly in the application as originally filed, ad are new matter.

Withdrawn Claim Rejections - 35 USC § 112 2nd¶ - Indefiniteness

2. The rejection of claim 17 under 35 U.S.C. 112, second paragraph, as being indefinite, as set forth in the previous Office Action, is **WITHDRAWN** in light of the amendment to claim 17.

Maintained Claim Rejections - 35 USC § 103

3. Claims 1, 4-6, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruano et al (1990) (as cited in the IDS) in view of Furlong et al and Ross et al (1998).

Ruano et al teaches a method for the analysis of haplotypes amplified from a single DNA molecule.

Ruano et al teaches that a nucleic acid sample is diluted to form a solution containing a single copy of the target molecule (p.6297 – Dilutions; Fig 3), relevant to step (a) of claims 1 and 4. Relevant to step (b) of claims 1 and 4, the reference further teaches the amplification of target DNA using a primer pair (GR5 and GR6) that amplifies a region comprising polymorphic sites (Fig 1; p.6297 – Target for amplification) and subsequent analysis of the polymorphic positions (a TG deletion, two SNPs, and a TaqI RFLP site) in the amplified fragment (Fig 4). Relevant to step (c) of claims 1 and 4, Ruano et al teaches the genotyping of sites amplified from the single molecule dilution target DNA (Fig 4) by southern hybridization and restriction digestion, thus genotyping nucleic acid regions that contain polymorphisms. Relevant to step (d) of claims 1 and 4, Ruano et al teaches that additional experiments are performed on sample DNA to resolve constituent haplotypes of heterozygous individuals (p.6298, right col., last paragraph; Fig. 3; Fig 4), and that each experiment followed the scheme present in Figure 3 of the reference, thus comprising steps (a)-(c) of claims 1 and 4. Relevant to step (e) of claims 1 and 4, the reference teaches that information regarding the individual genotypes is combined to determine the haplotype of the subject (Fig 4; p.6298 – Typing and direct haplotype determination of SMP products).

Regarding claims 4-6, Ruano et al teaches the analysis of a haplotype comprising polymorphic sites including single nucleotide polymorphisms and a dinucleotide insertion/deletion (Fig 1).

Ruano et al does not specifically teach an example in which a single molecule dilution is amplified in a multiplex PCR with at least four different primer pairs, relevant

to the limitation of step (b) of claims 1 and 4. Ruano et al does not specifically teach the analysis of 12-18 genotype replicas, relevant to the limitations of step (d) of claims 1 and. Ruano et al does not teach using primer extension and mass spectrometric detection to perform genotyping, relevant to the limitations of step (c) of claims 1 and 4.

Furlong et al teaches a method in which a single molecule dilution of a nucleic acid is amplified in a multiplex reaction for the determination of a haplotype (p.1192 – PCR of single sperm).

Regarding claim step (b) of claims 1 and 4, the reference specifically teaches the use of 4 different primer pairs to amplify four microsatellite regions on chromosome 9 (p.1192 – PCR primers; PCR of single sperm).

Regarding claim 20, Furlong et al specifically teaches primers that amplify a short amplicon of 149 bp (p.1192 – PCR primers), which is about 50 to about 100 base pairs.

Neither Ruano et al nor Furlong et al teaches the analysis of amplified polymorphic genotype markers using primer extension and mass spectrometric detection.

Ross et al teaches methods of multiplex genotyping using primer extension and mass spectrometry (p.1347, right col., lns.3-11). The reference teaches a method comprising the steps of simultaneous amplification of 12 polymorphic loci and subsequent multiplexed primer extension using oligonucleotide primers and ddNTPS (p.1350 – Experimental protocol, PCR). The reference further teaches analysis of the primer extension products by MALDI-TOF mass spectrometry (p.1350 – Experimental protocol, MS; Fig.2).

Regarding the limitation of step (d) of claims 1 and 4, Ruano et al teaches repetition of experimentation to resolve genotypes (p.6298 – right col., last paragraph), and further teaches that errors in haplotype determination should be held in check by analyzing replicate vials (p.6300, left col., lns.43-45). It would have been prima facie obvious to one of skill in the art at the time the invention was made to have modified the haplotype determination methods of Ruano et al to produce and analyze 12-18 replicas. One would have been motivated to create multiple genotype replicas based on the assertion of Ruano et al that such methods increase the accuracy of the analysis (p.6298 – right col., last paragraph; p.6300, left col., lns.43-45).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have combined the haplotype analysis methods of Ruano et al with the multiplex PCR methods of Furlong et al. One would have been motivated to do so because Furlong et al demonstrates the successful use of multiplex PCR for haplotype construction in the analysis of single molecules, and such a method would decrease the time and reagents required for the analysis of multiple polymorphic regions comprising a haplotype. One would have been further motivated to perform a multiplex PCR reaction based on the assertion of Ruano that distant segments of an intact template molecule can be analyzed by PCR with multiple primer pairs for direct haplotype determination (p.6300 – Discussion), which is a process that would be used in a multiplex reaction as taught by Furlong.

It would further have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the haplotype analysis methods of

Ruano et al in view of Furlong et al so as to incorporated the primer extension/mass spectrometry based genotype detection methods of Ross et al. One would have been motivated to use the methods of Ross et al based on the teachings of Ross et al that primer extension/mass spectrometry based methods eliminate excess handling and can resolve many possible genotypes/loci using a single non-fluorescent primer (p.1347, left col., ln.37).

Response to Remarks

Applicants have traversed the rejection of claims under 35 USC 103 as unpatentable in view of the teachings of Ruano et al, Furlong et al, and Ross et al. Applicants arguments (p.7-9 of Remarks) have been fully and carefully considered but are not found to be persuasive.

Applicants argue that the skilled artisan would not have combined the teachings of Ruano (single molecule PCR haplotyping) and/or Furlong (single molecule PCR-PCR haplotyping) with Ross (genotype determination using primer extension and mass spectrometry). Applicants argue that PCR amplification of a single template molecule is prone to errors, and that any such errors would be magnified using the sensitive detection methods (i.e. mass spectrometry) of Ross et al. Applicants argue that while the less sensitive methods of gel electrophoresis as taught by Ruano et al and Furlong et al are not overwhelmed by background noise from PCR errors, the skilled artisan would recognize that mass spectrometry is a very sensitive method sunject to more background noise because of the detection of errors as well as the intended peaks, where Ross et al does not teach such background noise due to using more original

nucleic acid template. Applicants argue that they have surprisingly found that mulitplex PCR of single molecule dilution can be accurately detected using mass spectrometry. This apparent argument of an unexpected result is not found to be persuasive. Initially it is noted that in their assertion of the 'anticipated problem of introduction of PCR errors into the reaction with single molecule starting material' (p. 8 of Remarks; with regard to analysis of an amplicon using primer extension and mass spectrometry) applicants have offered no specific arguments or evidence indicating that in fact the skilled artisan would not be motivated to combine the methods of the cited references. Applicants have provided no evidence as to what sort of template accuracy or heterogeneity is required for effective sequence detection using primer extension and mass spectrometry; and offered no evidence as to what level of 'introduction of PCR errors' the skilled artisan might expect in any PCR amplification; nor provided an analysis to indicate that the expected PCR error rate in the method of Ruano et al or Furlong et al would prevent the skilled artisan from using the detection methods of Ross. For example, the prior art of Wabuyele et al (2001) indicates that a Taq polymerase-based amplification reaction using a single template molecule provides excellent fidelity in replication (Table 1). Further relevant to the combination of amplification and polymorphism detection methods, it is noted that the Methods of Ruano et al are not merely 'gel electrophoresis methods'. Ruano et al uses, for example, RFLP analysis, which requires accurate replication of the restriction site for digestion.

Furthermore, with regard to Applicants' assertion of an unexpected result, it is noted that MPEP 716.02(c) provides guidance on considering such assertions, and specifically provides:

> Whether the unexpected results are the result of unexpectedly improved results or a property not taught by the prior art, the "objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence is offered to support." In other words, the showing of unexpected results must be reviewed to see if the results occur over the entire claimed range.

In the case of the instant application, with the exception of claim 20 the claims are generic with regard to the size of any amplicon, whereas the specification (paragraph [077] teaches:

> High PCR efficiency is mainly due to the high efficiency of amplification of very short amplicons (typically 100 bp) and the high sensitivity of MALDI-TOF mass spectrometric detection of DNA oligonucleotides.

And even with a 'very short' amplicon, it is noted that in a triplex genotyping assay (where the instant claims require at least four different primer pairs) apparently 50% (i.e. 6 of 12) of the reactions failed to provide the full analyzed haplotype (Table 1 of the instant specification).

Applicants also argue (p.9 of Remarks) that Ruano et al does not tech or suggest using single nucleotide polymorphisms for haplotype analysis. This argument is not found to be persuasive. As addressed in the rejection, Ruano et al provides the analysis of a haplotype that includes a single nucleotide polymorphism (e.g. see the legend of Fig 1 on page 6298 of Ruano et al).

With regard to newly presented claim 20, Applicants assert that amplification of short fragments is not disclosed in any of the cited references. As set forth in the

rejection, Furlong et al discloses primers that amplify a short amplicon that meets the limitations of claim 20.

The rejection as set forth is **MAINTAINED.**

4. Claims 3 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruano et al (1990) (as cited in the IDS) in view of Furlong et al and Ross et al (1998), and further in view of Drysdale et al (2000) (as cited in the IDS).

The teachings of Ruano et al in view of Furlong et al and Ross et al are applied to claims 3, and 9 as they were previously applied to claims 1 and 4-6.

Ruano et al in view of Furlong et al and Ross et al does not teach the comparison of a deduced haplotype with a haplotype from a control or a database of haplotypes to determine association of the haplotype with a biological trait, as required for claim 3, and step (e) of claim 9.

Drysdale et al teaches the use of β_2-adrenergic (β_2AR) receptor haplotypes in the prediction of response to albuterol (p.10486, left col., lns.6-8), which is a biological trait.

Regarding claim 3 and step (e) of claim 9 Drysdale et al teaches a collection of (β_2AR) haplotype pairs found in a cohort of asthmatics (p.10486, right col., lns.3-10; Table 2) (thus a database of haplotypes), as well as the association of the five most common haplotype pairs with patient response to albuterol (Fig.3; p.10487, left col., lns.1-25). The reference further teaches comparing a haplotype to the database of haplotypes and association data to determine association of the haplotype with a biological trait (Fig.3; p.10487, left col., lns.25-30).

It would have been prima facie obvious to one of skill in the art at the time the invention was made to have used the haplotype determination methods of Ruano et al in view of Furlong et al and Ross et al for the predictive analysis of haplotypes as taught by Drysdale et al. One would have been motivated to do so based on the assertion of Drysdale et al that haplotypes are more predictive of phenotype, and that individual SNPs may have poor predictive power as pharmacogenetic loci (p.10488, right col., lns.13-17). With specific regard to claim 11, it would be obvious to create and analyze numerous replicas, including producing 12-18 replicas, to increase the accuracy of the analysis. One would have been motivated to create multiple genotype replicas based on the assertion of Ruano et al that such methods increase the accuracy of the analysis (p.6298 – right col., last paragraph; p.6300, left col., lns.43-45).

Response to Remarks

Applicants' Remarks concerning the combination of the teachings of Ruano et al and Furlong et al (i.e. the combination of 12-18 replica genotypes and multiplexing using at least four primer pairs) have been addressed in the previous Response to Remarks. Furthermore it is noted that independent claim 9 requires only 'a multiplex amplification reaction with at least two primer pairs' (step (b) of claim 9. Thus Applicants arguments regarding the non-obviousness of requiring 'high multiplexing' of at least four primer pairs in combination with obtaining 12-18 replica genotypes is moot with regard to the limitations of claim 9.

The rejection as set forth is **MAINTAINED.**

5. Claims 12 and 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruano et al (1990) (as cited in the IDS) in view of Furlong et al and Ross et al (1998), and further in view of Rein et al (1998).

The teachings of Ruano et al in view of Furlong et al and Ross et al are applied to claims 12 and 15-17 as they were previously applied to claims 1 and 4-6.

Ruano et al in view of Furlong et al and Ross et al teaches a method for the analysis of haplotypes amplified in a multiplex PCR reaction from a single DNA molecule. Additionally, Ruano et al teaches the genotyping of sites amplified from the single molecule dilution target DNA by method including restriction digestion (Fig 3), and that information regarding the individual genotypes is combined to determine the haplotype of the subject (Fig 4; p.6298 – Typing and direct haplotype determination of SMP products). Thus, Ruano et al in view of Furlong et al and Ross et al provides steps (b)-(f) of claim 12, and steps (b)-(f) of claim 17. With particular regard to step (c) of claim 17, Ruano et al teaches the amplification of samples diluted to a single molecule concentration, as well as amplification of more concentrated samples (Fig 3; p.6297 – Standard PCR).

Ruano et al in view of Furlong et al and Ross et al does not teach an analysis of a nucleic acid sample that contains epigenetically modified nucleotides by specifically treating modified nucleotides (relevant to step (a) of claim 12) or digestion of a nucleic acid sample with a methylation sensitive restriction enzyme (relevant to step (a) of claim 17).

Rein et al teaches a method for the identification of 5-metyhlcytosine and related modifications in DNA genomes (Table 1; p.2255, right col., first full paragraph).

Regarding claim 12, Rein et al teaches methods for analysis of 5-methylcytosine (m^5C, which is a modified nucleotide) by treating genomic DNA with a composition that differentially affects epigentically modified nucleotides by converting non-methylated C to U, and not altering m^5C (p.2258 – Differential base modification by bisulfite), relevant to step (a) of claim 12, thus effectively creating polymorphisms (the content at a given nucleotide position can be a C if the position is methylated, or U (which behaves similar to a T in subsequent base pairing processes) if the position is nonmethylated) based on the epigenetic methylation modification (Fig 2).

Regarding claim 15, Rein et al teaches the analysis of 5-methylcytosine (m^5C), which is a methylated nucleotide (p.2258 – Differential base modification by bisulfite).

Regarding claim 16, Rein et al teaches the use of bisulfite for the treatment of a nucleic acid sample (p.2258 – Differential base modification by bisulfite; Table 1; p.2255, right col., ln.25).

Regarding claim 17, Rein et al teaches methods for analysis of methylated bases at specific DNA sites use modification-sensitive restriction endonucleases (Table 1; p.2257 - Modification-sensitive restriction endonucleases (MSREs); Fig 1). Relevant to step (a) of claim 17, the reference teaches the digestion of a sample with restriction enzymes that are sensitive to base modification (i.e. will not digest methylated sites) and restriction enzymes that require base modification (i.e. will only digest methylated sites) (p.2257, left col., lns.14-24; Fig 1). Relevant to step (f) of claim 17, Rein et al

teaches the analysis of the methylation dependent digestion of a sample by Southern analysis and PCR amplification (Fig 1; p.2258, left col., lns.15).

It would have been prima facie obvious to one of skill in the art at the time the invention was made to have modified the haplotype determination methods of Ruano et al in view of Furlong et al and Ross et al so as to have included the methylation analysis methods of Rein et al. One would have bee motivated to do so because Rein et al teaches that m^5C in the genomes of eukaryotic cells plays a role in a variety of processes (p.2255, left col., first paragraph of introduction). One would have been motivated to use the bisulfite treatment of Rein et al (relevant to claims 12, 15 and 16) because Rein et al teaches that such methods are highly sensitive, are amenable to rapid genomic sequencing, and provide positive display of m^5C (Table 1). One would have been motivated to use the MSRE method of Rein et al (relevant to claim 17) because Rein et al teaches that such methods provide a rapid analysis of large DNA regions, and are highly sensitive. With particular regard to step (f) of claim 17, the combination of the restriction enzyme digestion methods of Rein et al (as summarized in Fig 1 of Rein et al) and the haplotype determination methods of Ruano et al in view of Furlong et al and Ross et al would create a method where, for example, the DNA sample amplified by the multiplex PCR would be subjected to restriction digestion (as taught in Fig 1 of Rein et al) prior to amplification. Thus the determined haplotype would include polymorphic markers such as SNPs (determined by PCR as taught by Ruano et al) that are next to (e.g. the polymorphic sites would be adjacent to the cut site

determined by the action of an m^5C-requiring restriction enzyme) the methylation site analyzed by the restriction enzyme.

Response to Remarks

Applicants' traversal of the rejection of claims under 35 USC 103 as unpatentable in view of the teachings of Ruano et al, Furlong et al, Ross et al, and Drysdale et al (claims 3 and 9) or Rein et al (claims 12 and 15-17) is based on the alleged incompatibility of the teachings of Ruano et al and/or Furlong et al with Ross et al. This arguemtns has been addressed in the previous Response to Remarks in this Office Action. The Examiner maintains that there is no evidence to support Applicants' allegation that the skilled artisan would not be motivated to incorporate the methods of Ross et al into the methods rendered obvious by Ruano et al in view of Furlong et al.

The rejections as set forth are **MAINTAINED**.

Withdrawn Rejection
Double Patenting

6. The rejection of claims on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims of copending Application No. 10/542,043 in view of Furlong et al (1993) is **WITHDRAWN** in light of the Terminal Disclaimer filed in the instant application for the conflicting application.

7. The terminal disclaimer filed on 05/09/2008 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted on Application Number 10/542,043 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Conclusion

8. No claim is allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days.

Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Stephen Kapushoc/
Art Unit 1634

/Jehanne S Sitton/
Primary Examiner, Art Unit 1634